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Hemocoagulation disorders in burn injury (review). Part 1

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Abstract. ***Background.*** *In cases of severe, extensive burns, the compensatory hemocoagulation mechanisms are disrupted, triggering processes of microcoagulation, and hemostasis disorders take the form of disseminated intravascular coagulation (DIC).* ***Evidence collection.*** *A retrospective literature review was conducted using a spatial-vector descriptive model, supplemented by a manual selection of the articles cited therein. A total of 36 contemporary sources published within the last 10 years were selected, of which 88.9 % were published within the last 5 years.* ***Evidence synthesis.*** *The fibrinolytic system plays a vital role in maintaining vascular patency by regulating thrombus formation and mediating its lysis. Burn injury triggers early fibrinolytic activation and a pro- and anti-inflammatory imbalance. A higher degree of fibrinolytic activity has been documented with increasing burn size and depth, followed by the development of fibrinolytic inhibition, which intensifies with increasing time to hospital admission. Increased thrombogenesis and fibrinolytic activity are observed throughout the inpatient treatment of burn patients, as elevated concentrations of plasmin-α_2-antiplasmin, D-dimers and fibrin monomers have been detected during this period. It has been hypothesised that patients with burn injuries may exhibit three early fibrinolytic phenotypes, which may be associated with mortality to varying degrees. These include: hypofibrinolytic or fibrinolytic shutdown, normal or physiological, and hyperfibrinolytic. Secondary hyperfibrinolysis and pro- and anti-inflammatory imbalance typically occur in the early stages of severe burns, and both are closely associated with a poor prognosis. This process is accompanied by a rapid increase in D-dimer levels, a decrease in fibrinogen (consumption coagulopathy) and prolonged thrombin time. Burn-induced coagulopathy and DIC are independent pathologies. Sepsis-induced DIC is the most common challenge in the differential diagnosis of patients with burns and usually manifests 5–10 days after severe burn injury. DIC is divided into two distinct categories: compensated latent and uncompensated overt one.*

Keywords: *burn disease; coagulopathy; fibrinolysis; fibrinogen/fibrin degradation products; disseminated intravascular coagulation; diagnostic criteria*

Introduction

In cases of severe, extensive burns, the compensatory hemocoagulation mechanisms are disrupted, triggering processes of microcoagulation, and hemostasis disorders follow the pattern of disseminated intravascular coagulation (DIC syndrome), defined as a condition in which the vascular endothelium, blood and its components lose the ability to compensate for and restore the hemostatic response to injury, leading to multiple organ dysfunction as a result of thrombosis and hemorrhage.

Evidence collection

Literary sources were included in the study if they: 1) were published in Ukrainian, English or Chinese; 2) reported hemocoagulation disorders associated with burn disease and its complications; 3) provided information on the prevalence of coagulopathy in thermal burns and 4) used an observational study design (cohort or cross-sectional). The search for scientific literature was conducted using the CrossRef, Scopus, Google Scholar, Mesh and PubMed databases, covering the period from 2016 to 2026. A retrospective literature review was conducted using a spatial-vector descriptive model, supplemented by a manual selection of the articles cited therein. A total of 36 contemporary sources published within the last 10 years were selected, of which 88.9 % were published within the last 5 years.

Evidence synthesis

The fibrinolytic system plays an important role in maintaining vascular patency by controlling thrombus formation and mediating its lysis [1].

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The process of fibrinolysis is divided into two types: primary, or physiological, localised (the normal process that lyses a thrombus following vascular healing) and secondary, or pathological, generalised (the cleavage of clots resulting from pathological disorders, the action of medicinal products, etc.). Secondary hyperfibrinolysis and pro-/anti-inflammatory imbalance usually occur in the early stages of severe burns, and both are associated with a poor prognosis [2].

Early changes in fibrinolysis are of great importance for patients with severe burn injury [3]. Burn injury may be unique in this respect, as there is a strong correlation between the severity of lesions and the incidence of abnormal fibrinolysis. The activation of fibrinolysis may be associated with systemic inflammatory responses following burn injury, and establishing the relation between them should be promising and significant. Burn injury causes early fibrinolytic activation and a pro-/anti-inflammatory imbalance (within the first 24 hours following severe burns). A higher degree of fibrinolytic activity has been documented with an increase in the size and depth of the burn and the subsequent development of fibrinolytic inhibition, which intensifies with increasing time to hospital admission [1, 4–7].

In burn injury, tissue plasminogen activator (the primary activator of fibrinolysis) increases in parallel with plasminogen activator inhibitor-1 (PAI-1). Plasminogen concentrations decrease, reflecting plasmin activation. Concurrently with increased plasmin formation, the concentration of the main plasmin inhibitor (α_2-antiplasmin) decreases, as it forms complexes with plasmin to inactivate it [5].

Anticoagulant activity mediated by antithrombin and protein C is reduced in all patients with burn disease. It is believed that hyperfibrinolysis and systemic coagulopathy in patients with traumatic shock occur through the activation of protein C by thrombomodulin, characterised by a significant increase in soluble thrombomodulin in blood plasma and a decrease in protein C on the first day following mechanical trauma. However, it has been established that in patients with severe burns, thromomodulin levels remain within the normal range 12–24 hours after exposure to the thermal factor. This may indicate differences in the pathophysiological mechanism of fibrinolytic pathway activation in patients with burns and mechanical trauma, and the process of fibrinolytic system activation may differ at the pathophysiological level [4, 5].

An increase in thrombus formation and fibrinolytic activity is observed throughout the inpatient treatment of individuals with burns, as elevated concentrations of plasmin-α_2-antiplasmin, D-dimers (DDi) and fibrin monomers have been detected during this period. It appears that these processes alter the microstructure of the clot, leading to the formation of a weaker fibrin clot [8–10].

Patients with severe burns are considered *a priori* to be hyperfibrinolytic, given the elevated levels of tissue-type plasminogen activator on the first day following the burn. However, the initial activation of fibrinolysis is counterbalanced by a sustained increase in PAI-1 levels. Similar changes occur in patients with severe trauma and sepsis. It is believed that the rise in PAI-1 levels is an acute-phase response to both the trauma itself and the formation and deposition of fibrin [5].

Given the early activation of both pro- and antifibrinolytic mechanisms at the onset of the post-burn period, patients may develop specific fibrinolytic morphophysiological characteristics that may influence the outcome of the pathological condition. It has been hypothesised that patients with burn injuries can exhibit three early fibrinolytic phenotypes, which may be associated with mortality to varying degrees. These include: hypofibrinolytic or fibrinolytic shutdown (SD), normal or physiological, and hyperfibrinolytic (HF) [1, 6, 11, 12]. Different forms of coagulopathy with specific fibrinolytic phenotypes reflect differences in vascular permeability, endothelial activation and the development of tissue hypoperfusion [3].

Upon admission, HF can be identified within 1–2 hours of injury, whilst the delayed SD phenotype within 4 hours of the burn using thromboelastography [6].

On admission, 30.4 % of patients had the SD phenotype, 60.0 % had the physiological phenotype and 9.6 % had the HF phenotype. Patients with maladaptive SD or HF phenotypes were approximately 20 % more likely to have a larger total body surface area (TBSA) burn than those with the physiological phenotype ($p = 0.047$). Burns > 20 % TBSA were detected in a higher proportion of patients with pathological fibrinolysis (a combination of HF and SD) than burns covering a smaller area (54.8 versus 31.5 %; $p = 0.01$) [1, 6, 12].

An increase in the proportion of SD and a decrease in the percentage of the HF phenotype were observed during the first few hours following the burns. It was suggested that the development of the SD phenotype may be associated with tissue reperfusion during resuscitation following burn injury. Although SD at admission was not associated with increased mortality, delayed SD at 4 hours or later was characterised by an approximately eight-fold increase in mortality, regardless of the HF phenotype at admission [1].

The percentage of patients with the HF phenotype who survived decreased over time, whereas in those with SD it increased [1, 6].

Some patients have a greater innate resistance to tissue plasminogen activator. This may provide some protection against heart failure during the early post-burn period, but may also contribute to the development of delayed SD [6]. Following burn injury, a maladaptive fibrinolytic phenotype was associated with elevated levels of interleukins 6 and 10, as well as with mortality [12]. An increase in the international normalised ratio is observed in both hypofibrinolytic and hyperfibrinolytic phenotypes [1, 6].

The urokinase-type plasminogen activator receptor (uPAR) is a single-chain glycoprotein that binds to the cell membrane via a C-terminal glycosylphosphatidylinositol moiety. uPAR plays a significant role in fibrinolysis, where it helps regulate thrombus lysis; it is also crucial for maintaining normal blood flow and preventing excessive thrombus formation [13]. The urokinase receptor system is a key regulator of the interaction between inflammation, coagulation and fibrinolysis. uPAR and its ligand, namely urokinase-activated plasminogen (uPA), form a cell-surface-integrated multimolecular complex that performs pleiotropic functions (the ability to influence several physiological processes or phenotypic traits, often unrelated to one an-

other), thereby influencing the development of inflammatory, immune, coagulation and fibrinolytic reactions. uPAR is predominantly expressed in immune cells and is released from the cell surface via inflammatory stimulation to form soluble uPAR (suPAR), which can mediate similar processes by competing with uPAR for its ligand. The concentration of suPAR depends on the level of immune system activation and is currently recognised as a stable marker of immune activation and cellular inflammation [2, 13].

The soluble urokinase-type plasminogen activator receptor is involved in fibrinolysis and inflammation. suPAR is a non-specific marker of inflammation that reflects the level of immune system activation. Circulating suPAR levels correlated significantly with fibrinolytic activity, D-dimers, uPA, pro- and anti-inflammatory cytokines, the tumor necrosis factor α/interleukin-10 ratio, and platelet activation. The level of suPAR in the blood 48 hours after a burn is a valid prognostic biomarker for patients with severe burns. Activated platelets and their released products can significantly induce uPAR expression on the endothelial surface and serve as a source of suPAR in plasma. Megakaryocytes also express uPAR [2].

The uPA-uPAR system mediates the extrinsic fibrinolytic pathway. uPAR has no catalytic effect, but acts as a factor in localising plasminogen and uPA on the cell surface, thereby increasing the local concentration of the enzyme. The catalytic efficiency of uPA bound to uPAR is significantly higher than that of soluble uPA. Under the influence of proteases and inflammation, uPAR is cleaved from the cell surface, forming suPAR, which partially or significantly inhibits the binding of uPA to uPAR. In this case, suPAR acts as a competitive soluble receptor, attenuating the role of uPA as a cell-surface-bound plasminogen activator. DDi levels may reflect the extent of secondary hyperfibrinolysis. D-dimers are negatively correlated with suPAR, low levels of which in the blood may reflect secondary hyperfibrinolysis.

Burn injury can trigger the proliferation of immature myeloid cells in the bone marrow. Gr-1+ immature myeloid cells in the bone marrow are responsible for an increase in suPAR levels. However, severe burn injury can also lead to myelosuppression [2].

Secondary hyperfibrinolysis and pro- and anti-inflammatory imbalance typically occur in the early stages of severe burns, and both are closely associated with a poor prognosis. This process is accompanied by a sharp increase in D-dimer levels, a decrease in fibrinogen (consumptive coagulopathy) and prolonged thrombin time [2, 6].

Thromboelastography allows for the real-time assessment of whole blood coagulation function, including fibrinolysis, and offers an advantage over other tests in evaluating the balance between coagulation and fibrinolysis. A state of hypercoagulation and increased fibrinolysis is identified within the first 7 days following burn injuries using viscoelastic testing, which is not detected by standard coagulation tests. The identification and potential modification of fibrinolysis phenotypes based on early thromboelastographic monitoring may be useful in the management of patients with thermal injuries [1]. When used in combination with traditional coagulation markers, viscoelastic hemostatic tests enable more effective identification of specific coagulation phenotypes. These early changes reflect the evolving balance between profibrinolytic and antifibrinolytic mechanisms [6, 7, 11].

Elevated levels of DDi have been documented, reflecting the breakdown of fibrin or fibrinogen. Excessive activation of coagulation, combined with relatively suppressed fibrinolysis, leads to diffuse fibrin deposition, resulting in multiple organ dysfunction syndrome. Higher levels of fibrinolytic activation are associated with an increase in burn extent, multiple organ dysfunction syndrome and death [1, 6].

Trigger factors for burns showed a significant correlation with D-dimer levels, which were higher in cases of flame burns. Elevated DDi may reflect more extensive tissue destruction and more significant endothelial and microvascular damage, particularly in electrical and blast-related mechanisms, which are known to cause marked coagulation activation that is disproportionate to the obvious skin damage [14].

D-dimers are specific degradation products of fibrin, which form part of a thrombus. They are formed during the lysis of a blood clot under the influence of plasmin and non-specific fibrinolytics. The concentration of DDi in blood serum is proportional to the activity of fibrinolysis and the amount of fibrin being broken down. D-dimer is the most important marker of active thrombus lysis. Coagulopathy was frequently observed in patients with extensive burns, characterised by a significant increase in D-dimer levels during the first 28 days following the burn [1, 15].

Elevated DDi levels confirm the presence of early activation of the coagulation and fibrinolytic systems in patients with burns, highlighting its potential role as a biomarker of the systemic pathophysiological response following thermal injury [16]. Hypoxia-induced procoagulant signalling and hemolysis-related depletion of nitric oxide may enhance thrombin generation and fibrin turnover, thereby increasing blood D-dimer levels. However, early burn-induced coagulopathy (BIC) is heterogeneous, and the elevation in DDi may be influenced by several variables, both burn-related and non-burn-related [14].

In the early stages, D-dimer levels in adult patients with severe burns were mostly above the upper limit of normal, reflecting early activation of coagulation and fibrinolysis pathways caused by tissue damage and systemic inflammation during the acute phase of burn injury, particularly during the first 48 hours following the burn [4, 14, 17].

Although numerous studies have shown that D-dimer levels were elevated in burn patients after hospitalisation, given the local tissue damage and severe inflammatory response following burns, increased DDi is not specific and may be due to excessive fibrin clot formation, whereas local fibrin degradation leads to elevated levels of fibrinogen/fibrin degradation products (FDPs) [18].

The results of the current correlation analysis showed that increased D-dimer is dependent on various variables associated with venous thromboembolism; however, the association with these variables is primarily a marker of underlying systemic damage rather than a direct cause. The red blood cell distribution width and the coefficient of variation, which characterise the degree of anisocytosis, are accompanied by a greater increase in these parameters in the group with elevated D-dimer than in the group with normal D-dimer levels [14].

Elevated D-dimer reflects systemic inflammatory and coagulation responses involving hematological, immunological and organ dysfunction in acute burn injury [16].

In the group with increased D-dimer levels, a higher white blood cell count was observed compared to the group with normal D-dimer content ($p = 0.023$), further confirming the link between hypercoagulation and systemic inflammatory response. Based on correlation analysis, it was hypothesised that elevated D-dimer may be associated with impaired immune regulation and systemic organ dysfunction following acute burn injury. Increased DDi inversely correlated with burn-related anaemia (hemoglobin, red blood cell count and hematocrit; $r = -0.552$). In line with the negative correlation coefficients, hemoglobin, red blood cell count and hematocrit levels showed a tendency to decrease with increasing D-dimer. Higher DDi in acute burn injury correlates with a state of immune dysregulation [14]. Activation of the coagulation cascade is almost always present in infections, and the body's systemic inflammatory response is indicated by elevated levels of D-dimer in the plasma [16]. The percentage of basophils showed a general upward trend alongside rising DDi, and also demonstrated a significant positive correlation ($r = 0.688$) between the two. Conversely, the percentage of immunoglobulins and absolute immunoglobulin showed a gradual downward trend alongside rising D-dimer levels, which is also confirmed by a negative correlation coefficient for both parameters ($r = -0.472$ and $r = -0.497$, respectively), confirming the state of impaired immune regulation following burn injury [14].

Elevated DDi correlates with liver and kidney dysfunction after burn injury. Based on correlation analysis, liver function parameters, including aspartate aminotransferase and alanine aminotransferase, showed a very significant positive correlation ($r = 0.725$ and $r = 0.711$, respectively; $p = 0.001$) with D-dimer levels. A trend towards lower aspartate aminotransferase and alanine aminotransferase was observed from the group with lower DDi to the group with higher D-dimer. This may indicate liver dysfunction following burn injury. Urea also showed a tendency to increase with rising D-dimer, with the lowest levels in the group with D-dimer of 500–1000 ng/ml and the highest in the group with DDi ≥ 10,000 ng/ml [14].

Fibrinogen/fibrin degradation products and D-dimers are commonly used clinical markers for assessing fibrinolytic activity. Levels of both FDP and D-dimer were significantly elevated in patients with severe burns during the shock phase, with higher values in the group of deceased patients, although this was not statistically significant ($p > 0.05$) [18].

FDPs are formed as a result of fibrinogen degradation, and elevated levels indicate increased fibrinolysis. Fibrinogen/fibrin degradation products are fragments of the fibrinogen protein formed during its degradation by the enzyme plasmin. They are markers of fibrinolysis (the dissolution of blood clots) and increase during active blood clotting. Elevated FDP is used to confirm the presence of DIC [16]. An increase in the mean level of fibrin degradation products is also proportional to the severity of the burn (4.83, 8.12 and 15.48 μg/ml for mild, moderate and severe burns, respectively). During the first two weeks following the burn, only 7 % of patients had a minimal increase in FDP (mean 6.77 ± 0.07 μg/ml), whilst 93 % had levels at least four times higher than their maximum normal concentration (mean 41.33 ± 4.7 μg/ml) [19]. PAF is currently included in modern diagnostic criteria for DIC, as it not only indicates active fibrinolysis but also generally characterises the state of coagulation or fibrin formation [16, 19].

BIC and DIC are distinct pathologies. BIC encompasses trauma-induced DIC and secondary coagulopathy caused by anaemia, hemodilution, hypothermia and acidosis, i.e. it shares common features with the consequences of mechanical trauma and sepsis, such as activation of coagulation, reduced levels of anticoagulants and inhibition of fibrinolysis, making it indistinguishable from DIC. Severe BIC may progress to trauma-induced disseminated intravascular coagulation [20]. Burns covering more than 6 % TBSA usually cause systemic hypercoagulation, whereas severe burns covering more than 40 % TBSA predominantly cause consumption coagulopathy [8, 9].

All forms of DIC share common characteristics. Firstly, in most cases of DIC, thrombosis and bleeding coexist. Secondly, DIC is a dynamic process. Thirdly, damage to endothelial cells and activation of the systemic coagulation system form the basis of DIC. Fourthly, DIC is a triggering factor for multiple organ dysfunction syndrome [21].

DIC is a clinical and laboratory syndrome characterised by uncontrolled activation of intravascular blood coagulation, leading to a loss of normal hemostatic localisation, with a concomitant increased risk of microvascular and macrovascular thrombosis. A prolonged state of consumption and demand for coagulation resources is accompanied by DIC, which is very common in patients receiving infusion therapy, with hypothermia, hypoperfusion, acidosis and activation of the inflammatory cascade. Activation of the coagulation process leads to the formation of thrombin and fibrin, causing thrombosis of small and medium-sized vessels, consumption coagulopathy and organ dysfunction [5, 22, 23].

Over the years, many different terms have been used to describe coagulopathy in patients with severe burns. One of these is "systemic hypercoagulable state in burn patients", which is characterised by elevated levels of activated factor VII, the thrombin-antithrombin complex, PDF and PAI-1, combined with reduced levels of antithrombin and other natural anticoagulants [5].

Burn-related blood clotting abnormalities develop immediately following a burn injury or upon admission to the emergency department [23, 24].

The key laboratory indicators of intravascular activation of the hemostatic system and the development of DIC are thrombocytopenia and intravascular platelet aggregation, a decrease in antithrombin III levels, and an increase in activated partial thromboplastin time (aPTT). A decrease in aPTT 1–2 days after a burn in patients with a thermal injury index exceeding 90 may indicate the onset of the first phase of DIC, whilst aPTT elevated 3–5 days after thermal injury indicates an increased risk of bleeding, which may be fatal in patients with extensive burns, particularly those requiring surgical intervention [5, 22, 23, 25]. A reduction in plasma recalcification time 1–2 days after a burn injury demonstrates excessive hemostatic activity. A decrease in antithrombin III levels was observed in 70 % of patients during the first

3 days following the burn. This led to an intensification of the coagulation cascade, increasing the risk of venous thrombosis to 30 %. Accelerated blood clotting is observed within 1–2 days, and on days 3–4, consumption coagulopathy develops. Microthrombus formation and microcirculatory obstruction can develop throughout the circulatory system, predominantly in target organs (shock organs) — the brain, heart, lungs, kidneys, liver, gastrointestinal tract, etc. [21, 24, 25].

Sepsis-induced DIC is the most common challenge in the differential diagnosis of patients with burns and usually manifests 5–10 days after severe burn injury. Clinical symptoms are mild in the early stages and gradually progress in the middle and late stages [21]. DIC is characterised by abdominal distension, tachypnoea, vasomotor signs of hypotension and neurological deficits [26, 27]. Some clinical manifestations observed in patients with burns and DIC include thrombophlebitis (occurring in unusual locations), acute respiratory distress syndrome, acute kidney injury (decreased kidney function), central nervous system disorders (loss of consciousness and seizures), as well as a grey discolouration of the fingertips, toes or earlobes, and skin infarction and necrosis [23, 25].

Currently, most authors explicitly refer to "disseminated intravascular coagulopathy in burns" based on the typical hematological changes observed in DIC, in accordance with the more stringent criteria for it [5, 23].

The risk of developing DIC correlates directly with the severity and extent of burns [25]. Results from individual studies have shown that 30 % of patients with a TBSA > 25 % developed overt DIC within the first 24 hours of burn injury, with DIC occurring in 53.3 % of those who did not survive, compared to 6.7 % of survivors [5, 20].

DIC syndrome in severe burns is virtually identical to that seen in patients with sepsis, characterised by intravascular activation of coagulation and antifibrinolytic pathways, consumption of clotting factors, and depletion of coagulation-regulating proteins, leading to widespread fibrin deposition in the microvasculature [23, 28]. Increased consumption (depletion) of coagulation factors in DIC leads to their deficiency. Consumption coagulopathy results in the formation of microclots, which exacerbates tissue hypoperfusion and leads to organ failure [21, 28].

Coagulation disorders in patients with severe burns were most pronounced after one week; they may be caused by extensive burn injury (TBSA), excessive fluid therapy and sepsis, and may subsequently progress to DIC and even lead to death [20, 29].

Confirmed DIC syndrome is defined as a condition in which the vascular endothelium, blood and its components lose the ability to compensate for and restore homeostasis in response to injury, leading to multiple organ dysfunction as a result of thrombosis and hemorrhage [23].

DIC syndrome is divided into two distinct categories: compensated latent DIC and uncompensated overt DIC [30, 31]. Subclinical DIC (hypercoagulation, hypo-/hyperfibrinolysis) is a common occurrence in patients with burn injuries, and its severity increases exponentially with the severity of lesion. Presenting DIC occurs particularly frequently in critically ill patients with third-degree burns and extensive TBSA [19, 25, 30].

The use of different diagnostic criteria for DIC in patients with severe burns has resulted in a wide range of estimates of its occurrence (from 0.09 to 91.1 %) [5, 8, 9, 23, 24].

There are several diagnostic criteria for sepsis-associated DIC, including the standards of the Japanese Association for Acute Medicine (JAAM), the sepsis-induced coagulopathy (SIC) criteria, the International Society on Thrombosis and Haemostasis (ISTH) guidelines for overt DIC, and the Japanese Society on Thrombosis and Haemostasis criteria for DIC [21, 31, 32].

The ISTH criteria is a scoring system for diagnosing overt DIC. They analyse four parameters: platelets, D-dimers, prothrombin time and fibrinogen; the scores can be easily calculated using an online calculator. A total score of ≥ 5 points confirms the syndrome, whilst < 5 points indicates subclinical DIC. The ISTH criteria are most widely used to diagnose the uncompensated phase, i.e. overt DIC syndrome [21, 31–33].

The JAAM acute-phase criteria are used to diagnose the compensated phase of DIC. Three parameters are assessed (platelet count, fibrinogen/fibrin degradation products or D-dimers, and prothrombin index). A score of 3 is required to confirm DIC. All global coagulation tests, the criteria for systemic inflammatory response syndrome adopted in the JAAM standards, and their cut-off values were validated in parallel using scores on the Sequential Organ Failure Assessment and mortality rates. Patients with DIC had consistently higher Sequential Organ Failure Assessment scores during the first week following injury. The diagnostic threshold for compensated DIC according to the JAAM system was significantly higher than that of the other two [20, 31, 34].

A new assessment system known as SIC has now been proposed for the diagnosis of early sepsis-induced disseminated intravascular coagulation. The diagnostic and prognostic value of antithrombin was analysed.

The JAAM DIC criteria showed the highest rate of its diagnosis, whilst the risk of mortality in patients with SIC demonstrated a proportional increase with higher scores on the ISTH scale and the Chinese DIC assessment system. Low antithrombin activity (< 70 %) in patients with sepsis following a diagnosis of SIC predicted a very high 28-day mortality rate, almost twice that of the group with normal antithrombin activity (≥ 70 %). A trend towards reduced antithrombin activity following clinical interventions correlated with increased mortality. Adding antithrombin to the SIC scoring system may enhance its prognostic value [35, 36]. The reported incidence of SIC was approximately 60 % in patients with sepsis, which is twice that seen in cases of overt DIC. SIC had previously been diagnosed in almost all patients with overt DIC. The reported mortality rate for SIC was ≥ 30 %. Stratification of patients and their inclusion based on the presence of coagulopathy should be a mandatory requirement for any clinical trial targeting the coagulation system in sepsis. Early and simple diagnosis of DIC using a tool such as the SIC scoring system will allow for the adequate stratification of patients with sepsis according to the presence of coagulopathy and their subsequent appropriate inclusion in future clinical trials [32, 34].

In sepsis post burn injury, the progression of coagulopathy to DIC is associated with a poor prognosis [23]. Burn

patients with overt disseminated intravascular coagulation are at greater risk of developing organ failure and increased mortality. Early testing for blood coagulation may be useful for diagnosing and monitoring the progression of hemostatic disorders following severe burns, and the judicious use of blood products can help to prevent this [1, 6, 20, 29].

Other types of hemocoagulation disorders associated with burn injury will be discussed in Part 3 of this article.

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Розлади гемокоагуляції при опіковій хворобі (огляд). Частина 1

Резюме. ***Актуальність.*** При тяжких поширених опіках виникає зрив компенсаторних гемокоагуляційних механізмів, які запускають процеси мікрозгортання крові, а розлади гемостазу перебігають за типом дисемінованого внутрішньосудинного згортання крові (ДВЗ). ***Збір доказів.*** Ретроспективний відбір літератури проведено з використанням просторово-векторної описової моделі, доповненої ручним вибором статей, на які було надано посилання. Загалом обрано 36 сучасних джерел, опублікованих протягом останніх 10 років, з яких 88,9 % — за останні 5 років. ***Синтез доказів.*** Фібринолітична система відіграє важливу роль у підтриманні прохідності судин, контролюючи утворення тромбу й опосередковуючи його лізис. Опікова травма викликає ранню фібринолітичну активацію та про-/протизапальний дисбаланс. Було задокументовано вищий ступінь фібринолітичної активності зі збільшенням розміру і глибини опіку й подальшим розвитком фібринолітичного інгібування, що посилюється зі зростанням часу до моменту госпіталізації. Посилення тромбоутворення та фібринолітичної активності спостерігається протягом усього стаціонарного лікування комбустіологічних пацієнтів, оскільки за цей час виявлено підвищення концентрації плазміну-α_2-антиплазміну, D-димерів і фібринового мономеру. Висунуто гіпотезу, що пацієнти з опіковою травмою можуть демонструвати три ранні фібринолітичні фенотипи, різною мірою пов'язані зі смертністю. До них належать: гіпофібринолітичний або фібринолітичного вимкнення, нормальний або фізіологічний і гіперфібринолітичний. Вторинний гіперфібриноліз та про-/протизапальний дисбаланс зазвичай виникають на ранній стадії тяжких опіків, і обидва тісно пов'язані з поганим прогнозом. Цей процес супроводжується різким підвищенням рівнів D-димерів, зниженням фібриногену (коагулопатія споживання) та подовженням тромбінового часу. Опік-індукована коагулопатія та ДВЗ-синдром є незалежними патологіями. Спричинений сепсисом ДВЗ-синдром є найпоширенішою проблемою диференціально-діагностичного процесу в пацієнтів з опіками, що зазвичай проявляється через 5–10 днів після тяжкого опікового ураження. ДВЗ-синдром поділяють на дві окремі категорії: компенсований неявний та некомпенсований явний.

Ключові слова: опікова хвороба; коагулопатія; фібриноліз; продукти деградації фібриногену/фібрину; синдром дисемінованого внутрішньосудинного згортання крові; критерії діагностики